

REMARKS

Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, and 42-44 were pending in the application, with claims 42 and 43 withdrawn from present consideration. Upon entry of these amendments, Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, and 42-44 will be pending and under active consideration. Claims 1, 32, 33, 42, and 43 are independent.

Applicants submit respectfully that the amendments presented herein are supported fully by the claims and/or specification as originally filed and, thus, do not represent new subject matter.

Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present invention. Reconsideration and withdrawal of the rejections set forth in the above-identified Office Action are respectfully requested.

I. Rejections Under 35 U.S.C. § 112, First Paragraph

At paragraphs 6-11 of the Office Action, claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, and 44 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the invention at the time the application was filed, for the reasons of record. Applicants traverse respectfully.

With respect to the rejection made in paragraph 9 of the Office Action, Applicants respectfully direct Examiner's attention to page 21, lines 11-16, page 22, lines 2-3, and Fig. 2A. The examiner cites page 21, lines 11-16, of the specification as disclosing VNTRs but indicates that the disclosure does not enable the limitation that a first region of DNA to be sequenced

comprises VNTRs. Applicants point out that page 21, lines 15-16, noted by Examiner, recite that the “X_r region of the protein A gene of *S. aureus* has a variable length of variable number tandem repeats.” Page 22, lines 2-3 recite, “the X_r region of the *spa* gene can be sequenced in step 216” (please note that the *spa* gene is the protein A gene). Fig. 2A discloses step 216 as “Sequence first region of DNA.” Accordingly, Applicants submit respectfully that the combination of these three passages clearly and unambiguously discloses sequencing a first region of DNA that comprises VNTRs.

Applicants would respectfully point out further that the paragraph at page 21, lines 17-23, in the specification, which discloses SSRs, is applicable to VNTRs, and that the example studies are replete with disclosure of the use of repeat sequences in the inventive method. In fact, VNTRs are known in the art to be a type of SSR. Applicants would further note that that the van Belkum reference (1999, XP-002257260), at the first line of the abstract, indicates that VNTRs are also known as SSRs. In view of the above, Applicants submit respectfully that the rejection made in paragraph 9 of the Office Action has been overcome.

With respect to the rejection made in paragraph 10 of the Office Action, Applicants respectfully direct the Examiner’s attention to page 24, lines 17-18, pages 31-35, and the figures of the specification as filed. The Office Action alleges that the application discloses “comparing two isolates” but does not disclose comparing “at least two of a plurality of isolates,” as “comparing two isolates” means exactly two. Applicants submit respectfully that the application does, indeed, disclose comparing more than two isolates. For example, at page 24, lines 17-18, the specification recites, “server 119 determines the relatedness of the bacterial isolate to other isolates stored in the database.” According to the logic proposed in the Office Action, this

passage *must* refer to more than two isolates because the recitation mentions “the bacterial isolate” (1 isolate) and “other isolates” (at least two isolates) (emphasis added).

Furthermore, pages 31-35 disclose numerous examples of multiple isolate comparison. For example, page 31, line 7, recites, “suppose the X_r region of *three* bacterial isolates is sequenced” (emphasis added). This recitation is followed by a description of a comparison of all three. Page 33, lines 21-22, recites, “comparing the isolate to a wide range of historical bacterial isolate data.” Surely, a wide range of isolate data must represent a comparison of more than two isolates. Pages 34-35 describe an analysis of multiple isolates as disclosed in Fig. 5, which shows a comparison of data from 9 isolates. Fig 3, step 306, discloses comparing sequence data from one isolate to stored data from other isolates. Accordingly, Applicants submit respectfully that the rejection made in paragraph 10 of the Office Action has been overcome.

With respect to the rejection presented in paragraph 11 of the Office Action, Applicants respectfully direct the Examiner’s attention to page 13, lines 3-6, and Fig. 1 of the specification as filed. The rejection alleges that the limitation “transmitting. . . to each location having an outbreak problem” is not disclosed. Applicants submit respectfully that the application does, indeed, disclose transmitting a warning to each location having an outbreak problem. For example, page 13, lines 3-6, describing Fig.1, recite that the server “provides infection control information and warnings to hospital 102, physician’s office 106, long term care facility 110, laboratory 114, and other facilities involved with infection control via network 100.” The specification as filed notes in many places that any of these locations may have infectious disease outbreak problems. Accordingly, Applicants submit respectfully that the specification does disclose and enable the rejected claim and that the rejection of paragraph 11 has been overcome.

In view of the above, Applicants submit respectfully that the rejections have been overcome, and Applicants request respectfully that the 35 U.S.C. § 112, first paragraph, rejections of claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, and 44 be withdrawn.

II. The Rejections Under 35 U.S.C. § 103(a) Should Be Withdrawn

As a threshold matter, Applicants submit respectfully that the Office Action fails to describe sufficient motivation to combine the numerous references to reach Applicants' claimed invention. It is axiomatic in the patent law that motivation to combine references must be present within the references, themselves, and that without such motivation, the combination of references is improper. In particular, the Office Action seeks to combine *five different references* to reach the Applicants' invention in the rejection presented in paragraph 37. Applicants submit respectfully that even the combination of three references, as presented in the rejection presented in paragraph 14 of the Office Action, much less five references as noted above, requires that the Examiner bear a significant burden to show such motivation.

"It is impermissible to reconstruct the claimed invention from selected pieces of prior art absent some suggestion, teaching, or motivation in the prior art to do so." *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044, 1051-2, 5 USPQ2d 1434, 1438 (Fed. Cir. 1988). Absent some teaching, suggestion, or motivation found within the references that the emulsions claimed by Applicants are desirable, it cannot be inferred that Applicants' invention would have been obvious to one of ordinary skill in the art. "It is insufficient to select from the prior art the separate components of the inventor's combination, using the blueprint supplied by the inventor." *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1143, 227 USPQ2d 543, 551 (Fed. Cir. 1985).

Applicants request respectfully that the Examiner provide citations showing the motivation to combine the references as presented in the rejections under 35 U.S.C. § 103(a), or withdraw the rejections.

Notwithstanding the above, Applicants address the rejections under 35 U.S.C. § 103(a) as follows.

A. The Rejection Over Sloane In View Of Hoe And van Belkum

The Office Action, at paragraphs 14-36, rejects claims 1, 3-5, 7, 12-14, 16, 17, 25-34, 36, and 44 as allegedly being obvious over U.S. Patent No. 5,619,991 to Sloane (hereinafter, “Sloane”) in view of Hoe *et al.*, “Rapid Molecular Genetic Subtyping of Serotype M1 Group A *Streptococcus* Strains” *Emerging Infectious Diseases*, 5:254-263 (1999) (hereinafter, “Hoe”), in further view of van Belkum *et al.*, “Variable Number of Tandem Repeats in Clinical Strains of *Haemophilus influenzae*” *Infection and Immunity*, 65:5017-5027 (1997) (hereinafter, “van Belkum ‘97”) under 35 U.S.C. § 103(a) for the reasons of record. The Office Action alleges in sum that Sloane discloses an epidemiological database computer facility which collects and disburses medical, personal and epidemiological data. While the Office Action acknowledges that Sloane fails to teach the use of VNTR sequences for tracking the spread of infectious bacteria, the Office Action alleges that Hoe and van Belkum ‘97 cure these deficiencies. Applicants traverse respectfully.

Applicants submit respectfully that the novel system and method for tracking and controlling infections of the present invention is neither taught nor suggested by Sloane, either alone or in combination with Hoe and van Belkum ‘97. In particular, there is neither teaching nor suggestion in these references that 1) a network may be used to provide *warnings* regarding

epidemiological events or control the spread of disease, 2) a network may be used to transmit disease and geographical data related to the *pathogen* (as opposed to data about the patient, as disclosed in Sloane), or 3) comparing the *sequence of repeats* within VNTRs may be used to compare pathogens. Thus, Applicants submit respectfully that, as neither Hoe nor van Belkum '97 cure the deficiencies of Sloane with respect to the rejected claims of the present invention, the combination of the cited references fails to meet the threshold required for establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a).

The Sloane reference discusses the use of computer networks in the transfer of *patient* information. The Office Action asserts that this patient information can be any information, including sequence data. However, the present inventive network as claimed transfers information about the disease pathogen isolates taken from patient or even an inanimate object or location, not information about the patient himself as described by Sloane. As indicated by Sloane at column 8, lines 2-17, "patient transaction records" are the source of data analyzed by the Sloane method. The presently-claimed invention relates to sequence information from *pathogens*, including those found on objects as well as on persons, and Sloane neither teaches nor suggests this.

Applicants submit respectfully that Sloane is directed to diagnosing and treating patients (see abstract, line 1), while the presently-claimed invention seeks to prevent and/or control the spread of disease-causing bacteria and prevent outbreaks related to that spread. Accordingly, the epidemiology that can be conducted with the Sloane system is of an entirely different sort than that of the present invention. Furthermore, the Sloane system does not disclose providing warnings of potential disease outbreaks. As indicated by Sloane at column 8, lines 9-12, the Sloane system reports data to an outside organization (not part of the system) that may assist the

external organization (*i.e.*, the CDC) to provide reports or treatment options to affected persons or groups. Thus, Applicants submit respectfully that Sloane does not teach or suggest a system that provides warnings regarding epidemiological events.

With regard to non-sequence data transmitted by the system of Sloane, the system is described as transmitting data that identifies people in a geographical area that have the same illness in order to find an outbreak (see column 2, lines 30-39). Sloane's database contains geographic information about the patient, but Sloane only recites that the database might contain patient information such as the patient's address for billing purposes (see paragraph bridging columns 6-7)-- there is no suggestion that the Sloane database would track the current location of the patient or the current location of the pathogen. On the other hand, the presently-claimed invention determines an outbreak according to the location where a bacterial isolate is collected and using the genetic similarity of the pathogens as determined through sequence data comparison. Accordingly, Applicants submit respectfully that Sloane's disclosures are overbroad and do not suggest the same use of networking that the present invention uses.

The Office Action, as noted above, acknowledges that Sloane fails to teach the use of VNTR sequences for tracking the spread of infectious bacteria, the Office Action alleges that Hoe and van Belkum '97 cure these deficiencies. Applicants submit respectfully that neither Hoe nor van Belkum '97 teach or suggest the use of VNTR sequence data as disclosed and claimed by Applicants. As described at length in the present specification as filed, particularly at page 22, lines 20-21, page 24, lines 20-21, page 28, line 15, to page 30, line 4, the presently-claimed system uses a method of sequencing and comparing distinct "cassettes," or "repeat sequences," present in variable number and arrangement within repeat regions of the pathogenic

genome. The actual sequence of nucleotides within these cassettes is the basic element for comparison between bacterial isolates.

Van Belkum '97 and Hoe, contrary to the presently-claimed invention, *do not* use the sequence of the repeat cassettes to compare pathogens. Van Belkum '97 analyzes the *length and/or number* of repeat sequences in repeat regions and does not teach or suggest the analysis of the sequence within the repeat cassettes. For example, figures 1 and 2 of van Belkum '97 show the comparison of the total length of the repeat region for various isolates. Tables 3 and 4 show the number of repeats in various pathogen strains.

Hoe analyzes the sequences *between the cassettes* rather than the cassettes themselves. Figure 4 of Hoe, for example, shows the various differences in the spacer regions between DR (direct repeat) elements without analysis of the DR sequences, themselves. Again, the method of the present invention, which compares the sequence within repeat cassettes, is neither taught nor suggested by Hoe. Furthermore, it should be noted that direct repeat (DR) sequences *are not* VNTRs. DR sequences are well known in the art as having *identical* sequence in each of the repeated subunit cassette elements. Hoe showed that the spacer region between the elements may vary, but Hoe fails to disclose that the sequence of the cassette elements, themselves, might vary or be useful in an analysis for determining bacterial subtypes.

Accordingly, Applicants submit respectfully that neither Hoe nor van Belkum '97 teach or suggest Applicants' methods. As the Office Action admits that Sloane does not teach these methods, Applicants submit respectfully that the combination of Sloane with Hoe and van Belkum '97 does not disclose Applicants' methods. Accordingly, Applicants submit respectfully that the combination of Sloane with Hoe and van Belkum '97 does not meet the threshold required for establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a).

In view of the above, Applicants submit respectfully that the rejection of claims 1, 3-5, 7, 12-14, 16, 17, 25-34, 36, and 44 under 35 U.S.C. § 103(a) have been overcome, and Applicants request respectfully that the rejection of claims 1, 3-5, 7, 12-14, 16, 17, 25-34, 36, and 44 under 35 U.S.C. § 103(a) be withdrawn.

B. The Rejection Over Sloane In View Of Hoe, van Belkum, O'Brien, And Paradiso

The Office Action, at paragraphs 37-46, rejects claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, and 44 as allegedly being obvious over Sloane in view of Hoe and van Belkum '97 and further in view of O'Brien *et al.*, *Chest*, 112: 387-392 (hereinafter, "O'Brien") and U.S. Patent No. 6,404,340 to Paradiso *et al.* (hereinafter, "Paradiso") (in sum, the "Cited References"), under 35 U.S.C. § 103(a) for the reasons of record. In sum, the Office Action alleges that the combination of Sloane in view of Hoe and van Belkum '97 teaches all the limitations of the claims rejected above, but fails to teach the additional limitations of claims 8, 10, 11, 22-24, 35, and 38. The Office Action alleges that O'Brien and Paradiso cure these deficiencies. Applicants traverse respectfully.

Without acquiescing in the propriety of the allegations based upon the disclosures of O'Brien and Paradiso, Applicants submit respectfully that the novel systems and methods for tracking and controlling infections of the present invention are neither taught nor suggested by any of the Cited References, either alone or in any combination. As noted above, Sloane neither teaches nor suggests that 1) a network may be used to provide *warnings* regarding epidemiological events or control the spread of disease, 2) a network may be used to transmit disease and geographical data related to the *pathogen* (as opposed to data about the patient, as

disclosed in Sloane), or 3) comparing the *sequence of repeats* within VNTRs may be used to compare pathogens. As presented above, neither Hoe nor van Belkum '97 cure these deficiencies, and the Office Action does not allege that O'Brien and/or Paradiso cure these deficiencies. Thus, Applicants submit respectfully that combination of the Cited References fails to meet the threshold required for establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a).

With particular regard to claim 16, Applicants submit respectfully that, in addition to all of the reasons noted above, claim 16 is patentable over the cited references because none of the cited references discloses "treating the insertion or deletion of a repeat sequence as a single genetic event" as recited in claim 16.

Accordingly, Applicants submit respectfully that the rejection of Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, and 44 under 35 U.S.C. § 103(a) have been traversed, and Applicants request respectfully that the rejection of Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, and 44 under 35 U.S.C. § 103(a) be withdrawn.

AUTHORIZATION

Applicants believe there is no fee due in connection with this filing other than fees for the three month extension of time, which fees are authorized under the attached Petition For Extension Of Time Under 37 C.F.R. § 1.136(a). However, to the extent required, the Commissioner is hereby authorized to charge any fees due in connection with this filing to Deposit Account 19-5127 (Order No. 19124.0002) or credit any overpayment to same.

CONCLUSION

Applicants submit respectfully that the present application is in condition for allowance.

Favorable reconsideration, withdrawal of the rejections set forth in the above-noted Office

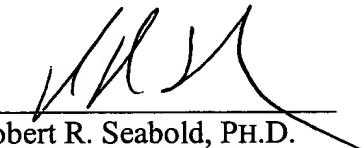
Action, and an early Notice of Allowance are requested.

If the Examiner feels that an interview would facilitate the prosecution of this application,

Applicants respectfully urge the Examiner to contact the undersigned directly at 202-295-8466.

In general, Applicants' undersigned attorney may be reached in our Washington, D.C. office by telephone at (202) 424-7500. All correspondence should be directed to our address given below.

Respectfully submitted,



Robert R. Seabold, Ph.D.
Registration No. 41,298
(202) 295-8466

Swidler Berlin Shreff Friedman
3000 K Street, NW, Suite 300
Washington, DC 20007
Telephone: (202) 424-7500
Facsimile: (202) 295-8478

Dated: October 14, 2004

9163203v2